REMARKS

By way of the present response, claims 1-2, 4-11, 13-20, 22-29, 31-38, 40-56 are pending. Claims 47-56 have been newly added and Claims 3, 12, 21, 30, and 39 have been cancelled without prejudice or disclaimer as allegedly being directed to a non-elected invention. Applicants have amended claims 1-2, 10-11, 19-20, 28-29, and 37-38 without prejudice or disclaimer. Applicants reserve the right to pursue the withdrawn claims in a continuing application. Support for the foregoing amendment can be found throughout the Specification and the claims as originally filed, for example, in the Specification at page 1, line 14-16; page 10-11; page 4, lines 16-23; page 5, line 3- page 13, line 19. No new matter has been added by way of the present amendment.

I. Restriction

Applicants respectfully disagree with the Office's final restriction requirement. However, solely in order to facilitate prosecution, claims 3, 12, 21, 30, and 39 have been cancelled without prejudice or disclaimer as directed to a non-elected invention.

II. Specification

Applicants have amended claim 28 in accordance with the Office's suggestions. As such, Applicants respectfully request withdrawal of the objections.

III. Rejection under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-46 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing. Office Action at page 6. In rejecting the claims, the Office alleges that "the description of one amino acid species (SEQ ID NO:1) is not adequate written description of the entire genus of functionally equivalent polypeptides which incorporate all variants and fragments with at least 50% sequence identity to a amino acid comprising the sequence of SEQ ID NO:1 (the base molecule)." Office Action at page 7.

Applicants note that the Office has withdrawn claims 3, 12, 21, 30, and 39 as allegedly being drawn to a nonelected invention or species. Office Action at page 2. As such, at the very least, claims 3, 12, 21, 30, and 39 were improperly rejected under 35 U.S.C. § 112, first paragraph. Appropriate correction is requested.

Applicants respectfully disagree with the Examiner's rejections under 35 U.S.C. § 112, first paragraph. However, solely in order to facilitate prosecution, Applicants have amended claims 1-2, 10-11, 19-20, 28-29, and 37-38 without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

In support of this rejection, the Office alleges that "the description of one amino acid species (SEQ ID NO:1) is not adequate description of an entire genus of functionally equivalent polypeptides which incorporate all variants and fragments with at least 50% sequence identity to an amino acid comprising the sequence of SEQ ID NO:1." Office Action at page 7. The Office goes on to assert that "the claims are drawn to a genus of polypeptides that are undefined." *Id.*. Applicants respectfully disagree with these assertions.

The standard for determining whether a claim drawn to a genus meets the written description requirement is clear. "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." *See Regents of the University of California v. Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406; M.P.E.P § 2163(II)(3)(a)(ii) (emphasis added). A "representative number of species" means that the species which are adequately described are representative of the entire genus. Description of a representative number of species does not require the description to be of such specificity that it would provide individual support for each species that the genus embraces. *Id.* Applicants have met this burden.

Initially, it is noted that the present claims are not drawn to a new genus of compounds, but rather to new uses of a generally known class of compounds. Nonetheless, what constitutes a "representative number" of species is an inverse function of the skill and knowledge in the art.

Capon v. Eshhar, 418 F.3d 1349 (Fed. Cir. 2005). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such specifics that it would provide individual support for each species that the genus embraces. "That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation." *Falkner v. Inglis*, 448 F.3d, 1357, 1366 (Fed Cir. 2006). Also relevant to the analysis is the claimed invention, and the context of the genus within the claimed invention.

In this regard, the present invention is directed to various methods a for treating nephropathy in a subject in need thereof, a method of treating or preventing End Stage Renal Disease in a subject in need thereof, a method of improving endothelial function in a subject in need thereof, a method of reducing proteinuria in a subject in need thereof, or a method of slowing progression of glomerulosclerosis in a subject in need thereof. As explained in the specification, in certain aspects it has been discovered that the administration of GLP-1 molecules, agonists, and variants to individuals in need thereof have the ability to treat the aforementioned disorders. Thus, the scope of the genus of GLP-1 compounds is viewed in the context of the claimed method, and the disclosure of species within the genus is understood by those skilled in the art based on the scope of teachings related to the claimed methods.

Within this context, any suitable GLP-1 compound may be useful in the invention, *e.g.*, useful as agents to treat nephropathy, treat End Stage Renal Disease (ESRD), improve endothelial function, reduce proteinuria, or slow progression of glomerulosclerosis. Extensive exemplary embodiments of known GLP-1 compounds with known activity in activating a GLP-1 receptor are discussed in the specification. Specification, for example, at page 6, line 18 - page 13, line 19. In this regard, it is noted that such GLP-1 compounds and agonist analogs were

generally known at the time of filing, as recognized by those skilled in the art. For instance, see U.S. Pat. Nos. 5,545,618, 5,574,008, and 5,118,666 cited on page 6 of the present specification.

Applicants thank the Examiner for indicating that the polypeptide of SEQ ID NO:1 satisfies the written description requirement. Office Action at page 8. Indeed, the Specification provides numerous GLP-1 species that are representative of the claimed genus. In addition, the specification provides for a wide-range of deletions, substitutions, and insertions may be made to the amino acid sequences of GLP-1 mutants. Specification, for example, at page 6, line 18 - page 13, line 19. The present application discloses numerous GLP-1 sequences and provides modified forms of the GLP-1 (7-34); (7-35); (7-35); (7-36); and (7-37). Specification at SEQ ID NO:1 - SEQ ID NO:11. When rejecting the claims under 35 U.S.C. § 112, first paragraph, the Office improperly ignores this large number of GLP-1 sequences and variants. In short, Applicants submit that the claimed genus is fully supported by the specification.

Further written description support for the claimed species can be found in the numerous patents and journal articles that are incorporated by reference in the specification. For example, US 5,120,712, a patent incorporated by reference in the instant specification, provides many possible GLP-1 derivatives, analogs, and fragments that are representative of the claimed genus. In meeting the written description requirement, "information incorporated is as much a part of the application as filed as if the text was repeated in the application, and should be treated as part of the text of the application as filed." MPEP 2163.07(b). This provides further support that Applicants were in possession of the claimed genus at the time the application was filed.

Applicants have provided sufficient guidance and working examples as to structural and functional characterization of the claimed GLP-1 species, *e.g.*, through extensive disclosure of GLP-1 sequences and representative variants. Specification, for example, at page 6, line 18 - page 13, line 19 and SEQ ID NO:1 - SEQ ID NO:11. Accordingly, Applicants submit that GLP-1 biologically active analogs, derivatives, variants, and fragments are sufficiently described in the specification as to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully submit that one skilled in the art would readily appreciate that Applicants, at the time of the filing of the present application, were in possession of the claimed genus and, therefore, have met the written description requirement. As such, it is submitted that

the claims comply with 35 U.S.C. §112, first paragraph, and withdrawal of this rejection is respectfully requested.

For at least the above reasons, Applicants respectfully request that the Office withdraws this rejection.

IV. Rejection under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-46 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way so as to enable those skilled in the art to make and/or use the invention commensurate in scope with the claims. Office Action mailed February 12, 2007 ("Office Action") at page 3. In rejecting the claims, the Office asserts that the specification "does not teach any functional variant, fragment, or derivative of the GLP-1 other than the full-length sequence of SEQ ID NO:1." *Id.*

At the outset, Applicants note that the Office has withdrawn claims 3, 12, 21, 30, and 39 as allegedly being drawn to a nonelected invention or species. Office Action at page 2. As such, at the very least, claims 3, 12, 21, 30, and 39 were improperly rejected under 35 U.S.C. § 112, first paragraph. Appropriate correction is requested.

Applicants respectfully disagree with the Examiner's rejections under 35 U.S.C. § 112, first paragraph. However, solely in order to facilitate prosecution, Applicants have amended claims 1-2, 10-11, 19-20, 28-29, and 37-38 without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

The Office has not met the evidentiary burden to impose an enablement rejection. A specification that discloses how to use a claimed invention "must be taken as in compliance with the enabling requirement of the first paragraph of § 112 unless there is reason to doubt the objective truth of the statements contained therein." *In re Brana*, 51 F.3d 1560, 1566, 34 U.S.P.Q.2d 1436, 1441 (Fed. Cir. 1995), *quoting In re Marzocchi*, 439 F.2d 220, 223, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971) (emphasis in original). The Office has provided neither evidence supporting the rejection nor any explanation of why the specification allegedly fails to enable the claimed invention.

As such, it is submitted that Applicants have provided considerable direction and guidance, and have presented working examples such that it is well within the level of ordinary

skill in the art to practice the invention without undue experimentation. The Office has not provided sufficient evidence to cast doubt on the guidance provided in the specification. Rather, the Office has provided generalizations regarding a lack of predictability in the art and the need for some experimentation.

Even assuming, *arguendo*, that the Office's generalization regarding the unpredictable state of the art is accepted, the conclusion that undue experimentation would be required to practice the claimed method is inconsistent with the current state of the law. Specifically, the law provides that experimentation is not necessarily undue simply because it is complex, if the art typically engages in such experimentation. *See In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174, (Int'l Trade Comm'n 1983) *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 U.S.P.Q. 428 (Fed. Cir. 1985).

Applicants disagree with the Office's assertion that the specification "does not teach any functional variant, fragment, or derivative of the GLP-1 other than the full-length sequence of SEQ ID NO:1." Office Action at page 4. The Office offers no support for this assertion. First, as explained, the present claims are not drawn to a new genus of compounds, but rather to new uses of a generally known class of compounds. The Office does not consider or address this point when rejecting the claims. Moreover, the specification is replete with examples of functional variants, fragments, and derivatives of GLP-1. Specification, for example, at page 6, line 18 - page 13, line 19. For example, given at least Formulas I-III as well as SEQ ID NO: 1 - SEQ ID NO:11, one of ordinary skill in the art having read the specification would have the ability to make nucleotide substitutions without undue experimentation. Specification, for example, at page 6, line 18 - page 13, line 19. Given this disclosure, one of ordinary skill in the art at the time the invention was made would also recognize which positions of the GLP-1 are amenable to mutations and conservative substitutions. Moreover, to the extent that any additional experimentation may be required, Applicant notes that the performance of routine and well-known steps cannot create undue experimentation even if it is laborious. *See In re Wands*, 858 F.2d at 737, 8 U.S.P.Q.2d at 1404; *In re Angstadt,* 537 F.2d 498, 504, 190 U.S.P.Q. 214, 218-219 (C.C.P.A. 1976).

Given this disclosure, Applicants respectfully submit that one of ordinary skill in the art

at the time the invention was made would have the ability to select variants, fragments, or derivatives of GLP-1 capable of being practiced with the claimed methods without undue experimentation. Applicants have sufficiently described the claimed invention such that one of skill in the art in light of the specification would be able to practice the invention commensurate in scope with the claims. Taken in combination, such disclosure provides adequate direction, including working examples, to teach the skilled artisan how to make and use the claimed invention without undue experimentation.

Accordingly, for at least these reasons, it is submitted that the claims are sufficiently enabled under 35 U.S.C. § 112, first paragraph, and withdrawal of this rejection is respectfully requested.

V. Rejection of Claims 1-46 under 35 U.S.C. § 112, Second Paragraph

A. Rejection of Claims 1-46

The Examiner asserts that claims 1-46 are rejected under 35 U.S.C. § 112, second paragraph, for allegedly failing to particularly point out and distinctly claim subject matter which Applicant regards as the invention. In rejecting these claims, the Examiner asserts that "it is not clear what are the meets and bounds of the claims since anything (since any variant derivative, or variant or mutation of a base molecule or a peptide having 50% identity) could be used." Office Action at page 9. Applicants disagree.

At the outset, Applicants note that the Office has withdrawn claims 3, 12, 21, 30, and 39 as allegedly being drawn to a nonelected invention or species. Office Action at page 2. As such, at the very least, claims 3, 12, 21, 30, and 39 were improperly rejected under 35 U.S.C. § 112, second paragraph. Appropriate correction is requested.

Applicants respectfully disagree with the Examiner's rejections under 35 U.S.C. § 112, second paragraph. However, solely in order to facilitate prosecution, Applicants have amended claims 1-2, 10-11, 19-20, 28-29, and 37-38 without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

Applicants respectfully submit that the Examiner's 35 U.S.C. § 112, second paragraph, indefiniteness rejection lacks any legal basis whatsoever. Applicants submit that the scope of the subject matter claimed is clear. Breadth of a claim is not to be equated with indefiniteness. *In re*

Miller, 441 F.2d 689 (CCPA 1971). If the scope of the subject matter embraced by the claims is clear, and if Applicants have not otherwise indicated that they intend the invention to be of a scope different from that defined in the claims, then the claims comply with 35 U.S.C. § 112, second paragraph. See MPEP § 2173.04.

Moreover, MPEP § 2173.02 states that the Examiner "should allow claims which define the patentable subject matter with a reasonable degree of particularity and distinctness. Some latitude in the manner of expression and the aptness of terms should be permitted even though the claim language is not as precise as the examiner might desire." In making this determination, MPEP § 2173.02 goes on to clarify that definiteness of claim language must be analyzed, not in a vacuum, but in light of the disclosure, prior art, and ordinary skill in the pertinent art. Given the above standard, Applicants respectfully submit that the claims are definite.

Applicants respectfully assert that the Examiner has not provided any legal rationale or explanation of why the claimed invention is indefinite. The specification provides numerous GLP-1 species that are representative of the claimed genus. Additionally, the present application discloses numerous GLP-1 sequences and provides modified forms of GLP-1 (7-34); (7-35); (7-35); (7-36); and (7-37). Specification at SEQ ID NO:1 - SEQ ID NO:11. Moreover, as currently presented in claims 2, 10, 20, 29, 38, and 47-51, GLP-1 is 90% or 95% identical to SEQ ID NO:1. In light of this, Applicants respectfully submit that the meets and bounds of the invention are clear. Office Action at page 7. That is, given the disclosure, one of ordinary skill in the art at the time the invention was made would have the requisite skill to practice the invention commensurate in scope with the claims. As such, the claimed invention satisfies 35 U.S.C. § 112, second paragraph, and the rejections should be withdrawn.

B. Rejection of Claims 1-9

The Office asserts that "[w]ith regard to claims 1-9, it is not clear how one can prevent a nephropathy in a subject having nephopathy." Office Action at page 9. Applicants respectfully disagree with the Office's rejections over claims 1-9. However, solely in order to facilitate prosecution, Applicants have amended claim 1 by deleting the term "preventing" without prejudice or disclaimer. As such, Applicants respectfully assert that the claim rejections are rendered moot.

C. Rejection of Claims 10-18

The Office also asserts that "[w]ith regard to claims 10-18, it is not clear **what** has to be prevented from progression to ESRD, as it is not clear what ERSD means, since it is not spelled-out in the claim." Office Action at page 9. Applicants respectfully disagree with the Office's rejections over claims 10-18. However, solely in order to facilitate prosecution, Applicants have adopted the Office's suggestion and have amended claim 10 by clarifying that the term "ERSD" refers to End Stage Renal Disease. As such, Applicants respectfully assert that the claim rejections are rendered moot.

D. Rejection of Claims 19-27

The Office also asserts that "[w]ith regard to claims 19-27 it is not clear what the meaning of the improvement of endothelial function is and as such the metes and bounds of the claims can not be established." Office Action at page 9. The improvement of endothelial function as a result of GLP-1 administration is described in Example 4. Specification at page 45, line 4 - page 46, line 2. As set forth in Figure 4, GLP-1 has the ability to help restore endothelial function in rats, thereby improving it relative to non-GLP-1 treated rats. Given at least this Example, Applicants respectfully submit that the meets and bounds are clear. That is, one of ordinary skill in the art at the time the invention was made would have the requisite skill to practice the invention commensurate in scope with the claims. Applicants submit that the claimed invention satisfies 35 U.S.C. § 112, second paragraph, and the rejections should be withdrawn.

VI. Rejection under 35 U.S.C. § 102

In rejecting claims 1-2, 4-11, 13-20, 22-29, 31-38, and 40-45, the Examiner asserts that WO 01/89554 ("Coolidge *et al.*") teach "a method of treatment, using GLP-1, of an individual with cardiac abnormalities consistent with ischemic heart disease." Office Action dated at page 10. Additionally, the Examiner contends that the "GLP-1 molecule of the invention of Coolidge *et al.* would bind and exert its action irrespective of the condition sought to be treated." *Id.* Applicants disagree.

In order for a claim to be anticipated, a reference must teach every element of the claim. MPEP § 2131. That is, "a claim is anticipated only if each and every element as set forth in the

claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

In rejecting the claims at issue, the Office asserts that "GLP-1 molecule of the invention of Coolidge *et al.* would bind and exert its action irrespective of the condition sought to be treated." Office Action at page 11. Applicants respectfully disagree. The claims at issue require a method for treating nephropathy in a subject in need thereof, a method of treating or preventing End Stage Renal Disease in a subject in need thereof, a method of improving endothelial function in a subject in need thereof, a method of reducing proteinuria in a subject in need thereof, or a method of slowing progression of glomerulosclerosis in a subject in need thereof. The Federal Circuit has directly addressed this issue of claim interpretation, and held that "the claims' recitation of a patient or a human 'in need' gives life and meaning to the preambles' statement of purpose. [. . .] The preamble is therefore not merely a statement of effect that may or may not be desired or appreciated. Rather, it is a statement of the intentional purpose for which the method must be performed." *Jansen v Rexall Sundown, Inc.*, 342 F.3d 1329, 1333 (Fed. Cir. 2003).

In accordance with proper claim interpretation, the present claims therefore require a method comprising the administration of the recited GLP-1 compounds for the intended purpose of treating nephropathy, treating or preventing End Stage Renal Disease, improving endothelial function, reducing proteinuria, or slowing progression of glomerulosclerosis, to a subject with a recognized need for such administration.

The Office further tries to support its 102 rejection by asserting that dosages and routes of administration disclosed in Coolidge overlap with the present application. Regardless of whether this assertion is correct, the Federal Circuit has held that use of a method for one condition does not necessarily preclude patentablity under 35 USC 102 for another condition. *Rapoport v Dement*, 254 F.3d 1053 (Fed. Cir. 2001) and *Jansen v Rexall Sundown, Inc.*, 342 F.3d 1329 (Fed. Cir. 2003). In *Rapoport*, the application was directed to the use of bispirone to treat sleep apnea in patients in need thereof. The cited art taught the use of bispirone in doses overlapping the claimed dose to treat anxiety, including treating anxiety in patients with sleep apnea. The Board of Patent Appeals and Interferences held, and the Federal Circuit affirmed, that the cited art did

not anticipate because it did not teach the administration of bispirone to treat sleep apnea. Likewise, *Jansen* involved the issue of whether a claim directed to the use of a combination of folic acid and vitamin B-12 to treat macrocytic-megaloblastic anemia in patients in need thereof was infringed by the use of the same combination within the claimed ranges to maintain blood homocysteine levels. Although *Jansen* involved infringement, the analysis of infringement or anticipation is the same. *Rapoport* at 1058. In finding no infringement, the court noted that the stated objective of the claim must be recognized and appreciated in interpreting the claims. *Jansen* at 1334.

Whatever else Coolidge *et al.* disclose or suggest, Coolidge *et al.* does not teach or even fairly suggest treating nephropathy, treating End Stage Renal Disease (ESRD), improving endothelial function, reducing proteinuria, or slowing progression of glomerulosclerosis. Moreover, Coolidge *et al.* does not disclose or suggest treating the aforementioned disorders with GLP-1.

To establish inherency "the Office must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990). To be found inherent in an anticipating reference, an unstated element must exist as a matter of scientific fact and flow naturally from the elements expressly disclosed in the prior art reference. *Hughes Aircraft Co. v. U.S.*, 8 U.S.P.Q.2d 1580, 1583 (Ct. Cl. 1988).

"The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Robertson*, 169 F.3d 743, 745, 49 U.S.P.Q.2d 1949, 1951 (Fed. Cir. 1999) (citations omitted); *see also Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354, 1367, 71 U.S.P.Q.2d 1081, 1091 (Fed. Cir. 2004). In other words, to support a rejection on the basis of inherency the Office must show that the patients with ischemic heart disease described in Coolidge, must, necessarily also have the conditions addressed in the present application. The fact that in some cases these two patient populations may overlap is simply insufficient to support an inherency rejection.

The Office has provided absolutely no evidence for the premise that the methods disclosed or suggested by Coolidge *et al.* would necessarily and without fail treat nephropathy or End Stage Renal Disease. Moreover, the Office has provided no evidence that Coolidge *et al.*

disclose methods of improving endothelial function, reducing proteinuria, or slowing progression of glomerulosclerosis. This should end the inquiry as it is the Office's burden to provide support that the methods disclosed or suggested by Coolidge *et al.* would necessarily and without fail treat the aforementioned disorders. All the Office has done is point to a few generic sentences directed to using GLP-1 to treat ischemic heart disease and extrapolated from those sentences that GLP-1 would inherently treat nephropathy or End Stage Renal Disease, improve endothelial function, reduce proteinuria, or slow progression of glomerulosclerosis. This rationalization is legally incorrect.

Again, whatever else Coolidge *et al.* may disclose, nothing in Coolidge *et al.* teaches or suggests the above-mentioned methods. Absent a teaching in this regard, one of skill in the art would simply find no motivation to perform a method as recited in the present claims for the specific intended purpose of such claims. The mere disclosure in Coolidge *et al.* of the administration of GLP-1 to treat ischemic heart disease does not amount to a teaching or suggestion of the claimed methods.

As the cited art does not disclose each and every element of the present independent claim, it is submitted that the claims are patentable over the prior art of record, and withdrawal of this rejection is respectfully requested.

VII. Rejection under 35 U.S.C. § 103

Claim 46 stands rejected under 35 U.S.C. § 103 as allegedly being obvious over WO 01/89554 ("Coolidge *et al.*") in view of US 2001/0016586 ("Guitard *et al.*"). In rejecting the claims, the Office has asserted that it would be *prima facie* obvious to modify the methods taught by Coolidge *et al.* to treat patients afflicted with hypertension, diabetes, and insulin resistance in view of Guitard *et al.* Office Action at page 12. Applicants disagree.

To establish a *prima facie* case of obviousness, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of skill in the art, to modify the reference or to combine reference teachings. There must also be a reasonable expectation of success. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on the applicant's disclosure. *In re Vaeck,* 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991).

Applicants respectfully assert that the Office has failed to establish a *prima facie* case of obviousness because the Office has not provided an adequate explanation of the suggestion or motivation to combine the teachings of Coolidge *et al.* with Guitard *et al.* Whatever else Coolidge *et al.* disclose, Coolidge *et al.* does not teach or even fairly suggest treating nephropathy, treating End Stage Renal Disease (ESRD), improving endothelial function, reducing proteinuria, or slowing progression of glomerulosclerosis. Guitard *et al.* does not provide motivation to modify Coolidge *et al.* by administering GLP-1 to patients afflicted with hypertension, diabetes, or insulin resistance. Moreover, taken together, neither Coolidge *et al.* nor Guitard *et al.* provide any specific motivation whatsoever for administering GLP-1 to a subject afflicted with hypertension, diabetes, or insulin resistance in a method for treating nephropathy.

"The mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990) (Claims were directed to an apparatus for producing an aerated cementitious composition by drawing air into the cementitious composition by driving the output pump at a capacity greater than the feed rate. The prior art reference taught that the feed means can be run at a variable speed, however the court found that this does not require that the output pump be run at the claimed speed so that air is drawn into the mixing chamber and is entrained in the ingredients during operation. Although a prior art device "may be capable of being modified to run the way the apparatus is claimed, there must be a suggestion or motivation in the reference to do so." 916 F.2d at 682, 16 USPQ2d at 1432.)." MPEP § 2143.01. As suggested by the Office, the motivation to combine Coolidge *et al.* with Guitard *et al.* "comes from the common etiology of the nephropathies." Office Action at page 12. The Office does not even explain in what way the method would be improved or why one of ordinary skill in the art at the time the invention was made would have the motivation to combine Coolidge *et al.* with Guitard *et al.* on the basis of "common etiology of the nephropathies." That is, common etiology is not sufficient motivation to combine Coolidge *et al.* with Guitard *et al.* "Rejections on obviousness ground cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning **with some rational underpinning** to support he legal conclusion of obviousness." *KSR Int'l. Co. v. Teleflex, Inc.*, No. 04-1350, slip op. at 14 (U.S.

April 30, 2007) quoting *In re Kahn* 441 F.3d 977, 988 (Fed. Cir. 2006) (emphasis added). Applicants therefore respectfully disagree with the Office's assertion that one of skill in the art would have been motivated to combine the teachings of Coolidge *et al.* with Guitard *et al.*

Applicants also respectfully assert that the Office has failed to establish a *prima facie* case of obviousness because there would have been no reasonable expectation of success, at the time the invention was made, in combining the teachings of Coolidge *et al.* with Guitard *et al.* At the outset, the Office does not even point out what the alleged reasonable success of combining Coolidge *et al.* with Guitard *et al.* would be. Rather, at best, the Office generally states that "it would have been obvious to one of skill in the art to modify the methods of Coolidge *et al.* with the diseases taught by Guitard *et al.* with a reasonable expectation of success." Office Action at page 12. Again, this is not enough. Without proper motivation and a reasonable expectation of success, the claims are improperly rejected under 35 U.S.C. § 103.

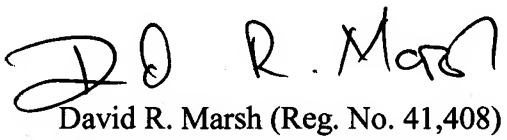
In conclusion, the Office has failed to meet even one of the requirements to establish a *prima facie* case of obviousness.

In light of these remarks, Applicant respectfully requests withdrawal of this rejection of claim 46 under 35 U.S.C. § 103 for purportedly being unpatentable over Coolidge *et al.* in view of Guitard *et al.*

CONCLUSION

In view of the above, each of the presently pending claims is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objection and rejections of the claims, and to pass this application to issue. The Examiner is encouraged to contact the undersigned at (202) 942-5186 should any additional information be necessary for allowance.

Respectfully submitted,



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